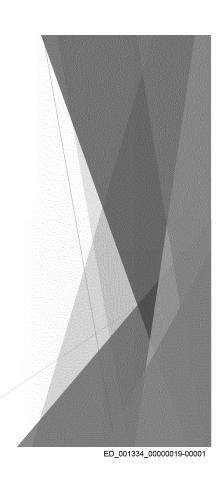
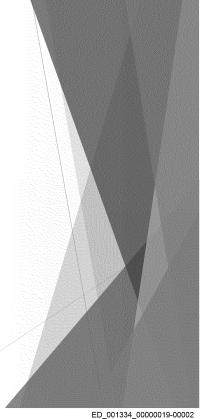
RD Briefing
on
New Fungicide
Active Ingredient
Flutianil
June 12, 2017



Agenda

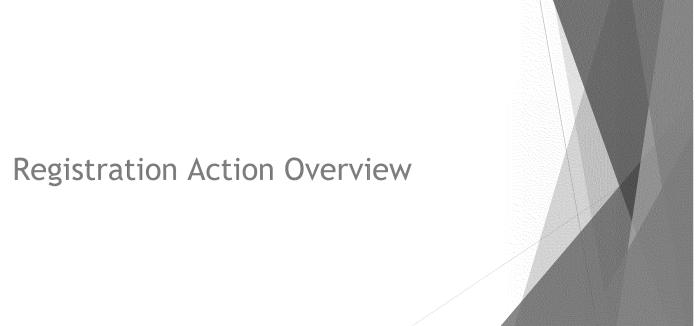
- Team Members
- Registration Action Overview (RD/FB)
- CITAB Assessments (RD/CITAB)
- Human Health Risk Assessment (HED/RAB6)
- Ecological Risk Assessment (EFED/ERB2)
- BEAD Assessment(BEAD/BAB)
- Proposed Registration Decision(RD/FB)



Flutianil OPP Team Members

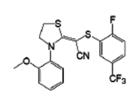
- RD
 - FB: Marcel Howard, Hope Johnson, Cynthia Giles-Parker
 - CITAB: Masih Hashim, John Redden, Shyam Mathur, PV Shah
- HED (RAB6)
 - Sheila Piper, Shalu Shelat, Yung Yang, Thomas Moriarty
- EFED (ERB2)
 - N.E. Federoff, James Lin, Karen Milians, Elyssa Arnold, Brian Anderson
- BEAD (BAB)
 - · Tara Chandgoyal, Colwell Cook, Monisha Kaul

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18cv0342 CBD v. EPA & FWS

What is Flutianil



- Class of chemistry
 - · Fungicide belonging to the thiazolidine chemical class
 - Chemical Name: 2*Z*-2-[2-fluoro-5-(trifluoromethyl)phenyl]sulfanyl- 2-[3-(2-methoxyphenyl) thiazolidin-2-ylidene]acetonitrile
- Mode of Action
 - Inhibits haustorium formation in the fungi and thus sporulation
 - Unique Mode of Action- "unknown" (FRAC U13)
- Pest control
 - Powdery Mildew: (Podosphaera leucotricha, Podosphaera xanthii, Podosphaera clandestina, Uncinula necator, Sphaerotheca macularis f. sp.fragariae).

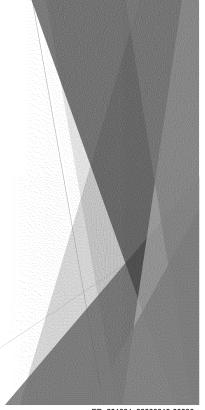
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Registration Action

- Type of Registration
 - Section 3 Registration- PRIA Code R020
 - Reduced Risk
 - Not a Global or Joint Review action (Japan MRLs exist)
- Current PRIA due date: 12/22/2017
- Registrant

18cv0342 CBD v. EPA & FWS

- OAT Agrio Co., Ltd.
- Proposed products
 - 1 technical 99.4% flutianil
 - 1 end-use EC product 4.7% flutianil



Notice of Receipt/Filing Publications

- Notice of Receipt published 3/16/2016
 - · A 14-page comment document by Center of Biological Diversity was submitted.
- Notice of Filing published 4/25/2016
 - The same 14-page comment document by Center of Biological Diversity was submitted.



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Proposed Use Profile

- Proposed uses
 - Apples, cantaloupes, cherries, cucumbers, grapes, strawberries, and summer squash
- Application rates
 - · Single maximum application rate: 0.04 lb ai/A
 - Maximum annual application rate: 0.16-0.20 lb ai/A.
 - Maximum of 4-5 applications per season. 2 seasons per year for squash and cucumber, 1 season per year for the remaining crops
- Application methods
 - · Broadcast ground or airblast ground equipment
- Significant Restrictions
 - Rotational crop restriction of 18 months for non-labeled crops

Reduced Risk Determination

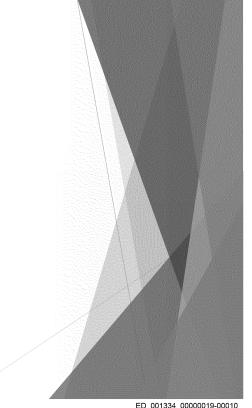
- Proposed as a Reduced Risk with initial application
- Reduced Risk Committee met on 6/7/2017
- Reduced risk status GRANTED in letter dated 6/15/2017 based on the following:
 - "Flutianil has a favorable human health risk profile when compared to the registered fungicides that is projected to displace in the market, as well as a novel mode of action that should fit well into integrated resistance management strategies for control of powdery mildew"

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Flutianil CITAB Assessments

Product Chemistry and Acute Toxicology

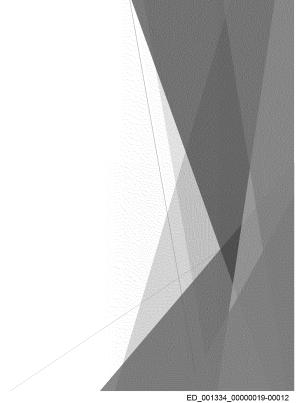
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Flutianil Product Specific Data

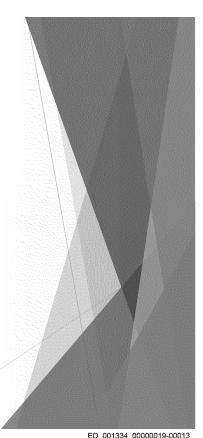
- Product Chemistry
 - Group A and Group B data acceptable
 - A new 5 batch analysis on the technical required once commercial production begins
- Acute Toxicology
 - Technical has low toxicity (Category IV for all routes of exposure and negative for skin sensitization. Signal word CAUTION.
 - End Use product also has low toxicity (Category IV for oral, acute dermal, dermal irritation, and inhalation) except for eye irritation which is Category II. Positive for skin sensitization. Signal word WARNING.

Flutianil HED Assessment



HED Proposed Use Summary

Product	Use	Application Method and Timing	Maximum Single Rate	Maximum Annual Rate
Flutianil (EC)	Apple, cherry, grape, and strawberry	Aerial and ground	0.04 lb ai/A (1-5 retreatments with a minimum interval of 7 days)	0.20 lb ai/A
		Fruiting Stage		
	Cantaloupe, cucumber, and summer squash	Aerial and ground Seeding Stage		



HED Flutianil Toxicity

- Toxicological Effects:
 - Oral (rat, mouse, dog): no significant adverse effects.
 - Dermal (rat, mouse, dog): no significant adverse effects
 - Inhalation (rat): increased lung weights in females and lung lesions in both sexes.
- No developmental or reproductive toxicity in rats; no sensitivity in rat pups compared to adults
- Not likely to be carcinogenic to humans
- No evidence of neurotoxicity or immunotoxicity

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HED Flutianil Endpoints

- Acute Dietary (All Populations): No endpoint attributable to a single dose.
- Chronic Dietary Endpoint: No adverse effects were seen in oral toxicity studies at

 1,000 mg/kg/day, including long-term studies in rats, mice, and dogs.
- Short-Term Incidental Oral Endpoint: An incidental oral risk assessment is unnecessary at this time, due to a lack of hazard.
- Dermal Endpoints: A dermal risk assessment is unnecessary at this time, due to a lack of hazard.
- Short- and Intermediate-Term Inhalation Endpoint: 28-day inhalation study in rats. The NOAEL (0.1 mg/L) is converted to HEC/HED based on the pulmonary effect; LOAEL = 1 mg/L. LOC for MOE<30.
- · Cancer: Classification: "Not likely to be Carcinogenic to Humans"

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HED Residue Chemistry Summary

- The registrant would like to harmonize with the currently established Japan MRLs.
 - No Codex or Canada MRLs are established
- HED is only concerned with tolerance enforcement and harmonizing with existing MRLs for international trade purposes.

Tolerance Summary	for Flutianil.		
Commodity	Proposed Tolerance (ppm)	HED- Recommended Tolerance (ppm)	Comments (correct commodity definition)
40 C	FR §180.XXX Tolera	nce for residues.	
Apple	0.2	0.15	
Apple, juice	0.03	_1	
Apple, wet pomace	2	0.30	
Cantaloupe	0.07	0.07	
Cherry	0.4	0.40	
Cucumber	0.02	0.20^{2}	
Grape	0.7	0.70	
Grape, juice	0.2	_1	
Grape, raisin	0.3	_1	
Squash	0.03	0.052	
Strawberry	0.3	0.50^{2}	
Not applicable	The processed commo	lities are covered und	er the row paric

Not applicable. The processed commodities are covered under the raw agricultural commodity (RAC) tolerances.
 EPA recommends harmonizing with Japan's MRL.

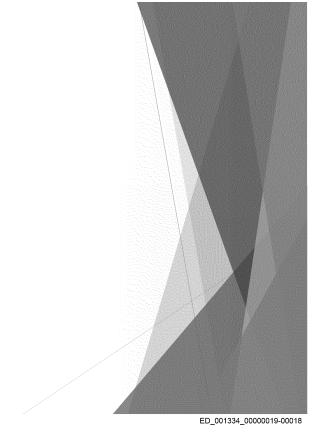
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HED Exposure Assessments Summary

- No dietary exposure assessments required
- No residential uses or exposures (including spray drift)
- No dietary, or residential assessments, therefore no aggregate assessment
- Occupational handler inhalation risk estimates are not of concern.
 - LOC for MOEs <30; inhalation MOEs range from 18,000 to 4,700,000
- No concerns for post application dermal exposures.
- 12-hour Re-entry Interval (REI) acceptable.

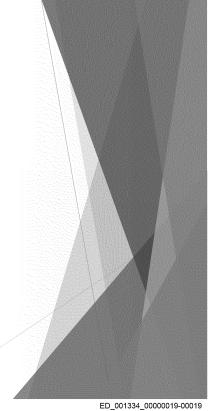
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Flutianil EFED Assessment



EFED Environmental Fate of Flutianil

- Transport and Mobility
 - Low solubility (0.0079 mg/L)
 - Slightly volatile (1.94 x 10-9 torr)
 - Low bioconcentration factor (BCF: 360 and 296)
 - Low mobility in soil (KOC: 17000 53000)



EFED Environmental Fate (cont.)

- Environmental Degradation
 - Hydrolytic Stable.
 - Aerobic and Anaerobic Soil T½ > 1000 days
 - Aerobic and Aquatic T½ 360 days to > 770 days
 - Aqueous Photolysis T½ 1.1 days
 - Soil Photolysis $T\frac{1}{2}$ 110 days
 - Field Dissipation $T\frac{1}{2}$ 52 to 398 days
 - No degradates of toxicological concern were identified

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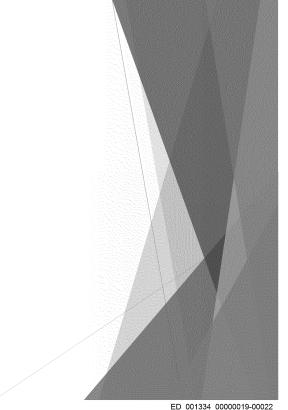
EFED Ecological Risk of Flutianil

- TGAI has low toxicity relative to expected exposures for terrestrial and aquatic organisms
- The EC formulation is more toxic than the active ingredient alone for freshwater fish and green algae.
- The degradates tested are less toxic than the parent compound.
- Conclusion: No risks of concern to any taxa were identified.
- [insert outstanding bee study statement]



Flutianil BEAD Assessment

Benefits & Public Interest Finding



BEAD/BAB Benefits & PIF

Benefits:

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- Efficacy generally superior than competitive fungicides (chlorothalonil, sulfur, myclobutanil, quinoxyfen, triflumizole, pyraclostrobin) for controlling claimed pests.
- New and unique mode of action with no known resistance in any powdery mildew.
 - Fungicide Resistance Action Committee (FRAC) Group U13.
- · No cross resistance with registered fungicides.
- · Likely to play a significant role in resistance management.

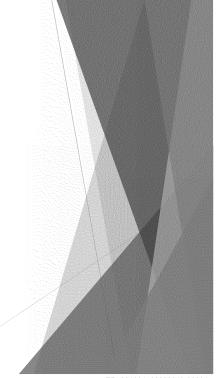
Public Interest Finding

• Flutianil meets the presumption of public interest because of its proposed registration for minor uses (cantaloupes, cherries, cucumbers, summer squash and strawberries).





Considerations, Proposed Decision and Timeline



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Registration Consideration Summary

- Reduce risk status granted
- Human health assessment no risks of concern
- Ecological assessment risk to all taxa are below the Agency's LOCs for both listed species as well as non-listed species
- No cross-resistance against existing fungicides and appears to control virulent fungal pest (powdery mildew)
- Unique mode of action (FRAC U13)
- Likely to play a significant role in resistance management
- No synergy claims made (per Registrant)

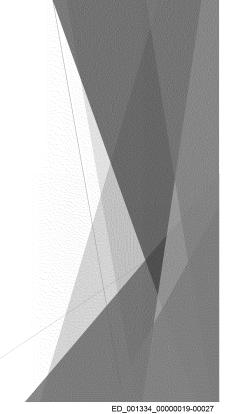
Proposed Label Requirements/Mitigation

- Rotational Crop Restriction
 - For any crop other than cantaloupes, cucumbers, summer squash, and strawberries, the rotation interval is a minimum of 18 months after the latest application of the end-use product
- Clarification on label to restrict against application methods not requested
 - · Aerial, chemigation, greenhouse

Proposed Decision

Conditional Registration requiring the following:

- New 5-batch analysis under commercial production
- 2. 21-day chronic larval honey bee data



Timeline

- The PRIA due date was previously renegotiated from 4/21/2016 to 12/22/2017 due to late submission of leptocheirus data.
- Upcoming Briefings
 - DD briefing [late June-early July]
 - OD briefing 7/18/2017
 - Proposed Decision Document drafted
 - Under OPP Team comment period currently
- Final Rule currently being drafted
- Peer Review goal of June 2016
- Public comment period goal beginning August 2017
- Final registration decision goal of 11/27/2017

